

Applicant : Shigeaki Kato et al.  
Serial No. : 09/489,198  
Filed : January 20, 2000  
Page : 3

Attorney's Docket No.: 06501-054001 / C1-901PCT-  
US

REMARKS

Applicants hereby submit that the enclosures fulfill the requirements under 37 C.F.R. §1.821-1.825. The amendments in the specification merely insert the paper copy of the Sequence Listing and sequence identifiers in the specification. In particular, the description of Figure 4 has been amended to insert a sequence identifier. No new matter has been added.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment.

Please apply any charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date:

Aug. 31, 2001

Janis K. Fraser, Ph.D., J.D.  
Reg. No. 34,819

Fish & Richardson P.C.  
225 Franklin Street  
Boston, Massachusetts 02110-2804  
Telephone: (617) 542-5070  
Facsimile: (617) 542-8906

Applicant : Shigeaki Kato et al.  
Serial No. : 09/489,198  
Filed : January 20, 2000  
Page : 4

Attorney's Docket No.: 06501-054001 / C1-901PCT-  
US

**“Version With Markings to Show Changes Made”**

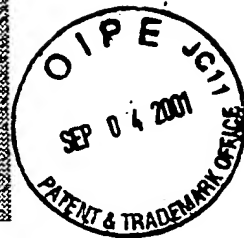
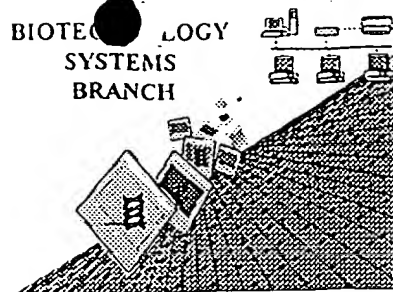
In the specification:

Paragraph beginning at page 22, line 19, has been amended as follows:

Figure 4 shows the putative amino acid sequenec of CYP1AD (SEQ ID NO:1). The first methionine is assigned as position 1. Asterisk indicates the terminal codon. Putative mitochondria targeting signal is surrounded by square. Underline indicates sterol binding domain. Dotted underline indicates hem-binding domain.

## RAW SEQUENCE LISTING ERROR REPORT

BIOTECHNOLOGY  
SYSTEMS  
BRANCH



The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 09/489,198

Source: 1646

Date Processed by STIC: 6-14-01

RECEIVED

JUL 09 2001

TECH CENTER 1600/2900

RECEIVED

SEP 07 2001

TECH CENTER 1600/2900

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.

PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:

- 1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,
- 2) TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY

FOR CRF SUBMISSION QUESTIONS, PLEASE CONTACT MARK SPENCER, 703-308-4212.

FOR SEQUENCE RULES INTERPRETATION, PLEASE CONTACT ROBERT WAX, 703-308-4216.

PATENTIN 2.1 e-mail help: [patin21help@uspto.gov](mailto:patin21help@uspto.gov) or phone 703-306-4119 (R. Wax)

PATENTIN 3.0 e-mail help: [patin3help@uspto.gov](mailto:patin3help@uspto.gov) or phone 703-306-4119 (R. Wax)

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE CHECKER VERSION 3.0 PROGRAM, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW:

### Checker Version 3.0

The Checker Version 3.0 application is a state-of-the-art Windows based software program employing a logical and intuitive user-interface to check whether a sequence listing is in compliance with format and content rules. Checker Version 3.0 works for sequence listings generated for the original version of 37 CFR §§1.821 - 1.825 effective October 1, 1990 (old rules) and the revised version (new rules) effective July 1, 1998 as well as World Intellectual Property Organization (WIPO) Standard ST.25.

Checker Version 3.0 replaces the previous DOS-based version of Checker, and is Y2K-compliant. Checker allows public users to check sequence listings in Computer Readable form (CRF) before submitting them to the United States Patent and Trademark Office (USPTO). Use of Checker prior to filing the sequence listing is expected to result in fewer errored sequence listings, thus saving time and money.

Checker Version 3.0 can be down loaded from the USPTO website at the following address:

<http://www.uspto.gov/web/offices/pac/checker>



## Raw Sequence Listing Error Summary

### ERROR DETECTED    SUGGESTED CORRECTION

SERIAL NUMBER: 09/489,198

ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE

- 1      Wrapped Nucleics    The number/text at the end of each line "wrapped" down to the next line. This may occur if your file  
    Wrapped Aminos    was retrieved in a word processor after creating it. Please adjust your right margin to .3; this will  
    prevent "wrapping."
- 2      Invalid Line Length    The rules require that a line not exceed 72 characters in length. This includes white spaces.
- 3      Misaligned Amino    The numbering under each 5<sup>th</sup> amino acid is misaligned. Do not use tab codes between numbers;  
    Numbering    use space characters, instead.
- 4      Non-ASCII    The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. Please  
    ensure your subsequent submission is saved in ASCII text.
- 5      Variable Length    Sequence(s)      contain n's or Xaa's representing more than one residue. Per Sequence Rules,  
    each n or Xaa can only represent a single residue. Please present the maximum number of each  
    residue having variable length and indicate in the <220>-<223> section that some may be missing.
- 6      PatentIn 2.0    A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid  
    "bug"    sequences(s)     . Normally, PatentIn would automatically generate this section from the  
    previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to  
    the subsequent amino acid sequence. This applies to the mandatory <220>-<223> sections for  
    Artificial or Unknown sequences.
- 7      Skipped Sequences    Sequence(s)      missing. If intentional, please insert the following lines for each skipped sequence:  
    (OLD RULES)    (2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)  
    (i)    SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading)  
    (xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)  
    This sequence is intentionally skipped  
  
    Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to include the skipped sequences.
- 8      Skipped Sequences    Sequence(s)      missing. If intentional, please insert the following lines for each skipped sequence.  
    (NEW RULES)    <210> sequence id number  
    <400> sequence id number  
    000
- 9 ✓      Use of n's or Xaa's    Use of n's and/or Xaa's have been detected in the Sequence Listing.  
    (NEW RULES)    Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present.  
    In <220> to <223> section, please explain location of n or Xaa, and which residue n or Xaa represents.
- 10      Invalid <213>    Per 1.823 of Sequence Rules, the only valid <213> responses are: Unknown, Artificial Sequence, or  
    Response    scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or  
    is Artificial Sequence
- 11      Use of <220>    Sequence(s)      missing the <220> "Feature" and associated numeric identifiers and responses.  
    Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or  
    "Unknown." Please explain source of genetic material in <220> to <223> section.  
    (See "Federal Register," 06/01/1998, Vol. 63, No. 104, pp. 29631-32) (Sec. 1.823 of Sequence Rules)
- 12      PatentIn 2.0    Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file,  
    "bug"    resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence  
    listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.

# RECEIVED

SEP 07 2001

TECH CENTER 1600/2900

Page 1 of 6

#10  
Cmey  
1-9-10  
1646



RAW SEQUENCE LISTING  
PATENT APPLICATION: US/09/489,198

DATE: 06/14/2001  
TIME: 10:13:12

Input Set : A:\Sequence.txt  
Output Set: N:\CRF3\06142001\I489198.raw

3 <110> APPLICANT: CHUGAI SEIYAKU KABUSHIKI KAISHA.  
5 <120> TITLE OF INVENTION: Gene screening method using nuclear receptor  
7 <130> FILE REFERENCE: C1-901PCT  
C--> 9 <140> CURRENT APPLICATION NUMBER: US/09/489,198  
C--> 10 <141> CURRENT FILING DATE: 2000-01-20  
12 <150> PRIOR APPLICATION NUMBER: JP 09/212624  
W--> 13 <151> PRIOR FILING DATE: 1997-7-22 → 1997-07-22  
15 <160> NUMBER OF SEQ ID NOS: 4  
17 <170> SOFTWARE: PatentIn Ver. 2.0

Does Not Comply  
Corrected Diskette Needed  
See pg. 1, 2, 5

## ERRORED SEQUENCES

19 <210> SEQ ID NO: 1  
20 <211> LENGTH: 507  
E--> 21 <212> TYPE: RPT → Valid <212> responses:  
22 <213> ORGANISM: Mus musculus  
24 <400> SEQUENCE: 1  
25 Met Thr Gln Ala Val Lys Leu Ala  
26 1 5  
27 Ser Arg Val Phe His Arg Ile His Leu Pro Leu Gln Leu Asp Ala Ser  
28 10 15 20  
29 Leu Gly Ser Arg Gly Ser Glu Ser Val Leu Arg Ser Leu Ser Asp Ile  
30 25 30 35 40  
31 Pro Gly Pro Ser Thr Leu Ser Phe Leu Ala Glu Leu Phe Cys Lys Gly  
32 45 50 55  
33 Gly Leu Ser Arg Leu His Glu Leu Gln Val His Gly Ala Ala Arg Tyr  
34 60 65 70  
35 Gly Pro Ile Trp Ser Gly Ser Phe Gly Thr Leu Arg Thr Val Tyr Val  
36 75 80 85  
37 Ala Asp Pro Thr Leu Val Glu Gln Leu Leu Arg Gln Glu Ser His Cys  
38 90 95 100  
39 Pro Glu Arg Cys Ser Phe Ser Ser Trp Ala Glu His Arg Arg Arg His  
40 105 110 115 120  
41 Gln Arg Ala Cys Gly Leu Leu Thr Ala Asp Gly Glu Glu Trp Gln Arg  
42 125 130 135  
43 Leu Arg Ser Leu Leu Ala Pro Leu Leu Leu Arg Pro Gln Ala Ala Ala  
44 140 145 150  
45 Gly Tyr Ala Gly Thr Leu Asp Asn Val Val Arg Asp Leu Val Arg Arg  
46 155 160 165  
47 Leu Arg Arg Gln Arg Gly Arg Gly Ser Gly Leu Pro Gly Leu Val Leu  
48 170 175 180  
49 Asp Val Ala Gly Glu Phe Tyr Lys Phe Gly Leu Glu Ser Ile Gly Ala  
50 185 190 195 200  
51 Val Leu Leu Gly Ser Arg Leu Gly Cys Leu Glu Ala Glu Val Pro Pro  
52 205 210 215  
53 Asp Thr Glu Thr Phe Ile His Ala Val Gly Ser Val Phe Val Ser Thr

## RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/489,198

DATE: 06/14/2001

TIME: 10:13:12

Input Set : A:\Sequence.txt

Output Set: N:\CRF3\06142001\I489198.raw

```

54          220          225          230
55 Leu Leu Thr Met Ala Met Pro Asn Trp Leu His His Leu Ile Pro Gly
56          235          240          245
57 Pro Trp Ala Arg Leu Cys Arg Asp Trp Asp Gln Met Phe Ala Phe Ala
58          250          255          260
59 Gln Arg His Val Glu Leu Arg Glu Gly Glu Ala Ala Met Arg Asn Gln
60 265          270          275          280
61 Gly Lys Pro Glu Glu Asp Met Pro Ser Gly His His Leu Thr His Phe
62          285          290          295
63 Leu Phe Arg Glu Lys Val Ser Val Gln Ser Ile Val Gly Asn Val Thr
64          300          305          310
65 Glu Leu Leu Leu Ala Gly Val Asp Thr Val Ser Asn Thr Leu Ser Trp
66          315          320          325
67 Thr Leu Tyr Glu Leu Ser Arg His Pro Asp Val Gln Thr Ala Leu His
68          330          335          340
69 Ser Glu Ile Thr Ala Gly Thr Arg Gly Ser Cys Ala His Pro His Gly
70 345          350          355          360
71 Thr Ala Leu Ser Gln Leu Pro Leu Leu Lys Ala Val Ile Lys Glu Val
72          365          370          375
73 Leu Arg Leu Tyr Pro Val Val Pro Gly Asn Ser Arg Val Pro Asp Arg
74          380          385          390
75 Asp Ile Arg Val Gly Asn Tyr Val Ile Pro Gln Asp Thr Leu Val Ser
76          395          400          405
77 Leu Cys His Tyr Ala Thr Ser Arg Asp Pro Thr Gln Phe Pro Asp Pro
78          410          415          420
79 Asn Ser Phe Asn Pro Ala Arg Trp Leu Gly Glu Gly Pro Thr Pro His
80 425          430          435          440
81 Pro Phe Ala Ser Leu Pro Phe Gly Phe Gly Lys Arg Ser Cys Ile Gly
82          445          450          455
83 Arg Arg Leu Ala Glu Leu Glu Leu Gln Met Ala Leu Ser Gln Ile Leu
84          460          465          470
85 Thr His Phe Glu Val Leu Pro Glu Pro Gly Ala Leu Pro Ile Lys Pro
86          475          480          485
87 Met Thr Arg Thr Val Leu Val Pro Glu Arg Ser Ile Asn Leu Gln Phe
88          490          495          500
89 Val Asp Arg
90 505

```

92 &lt;210&gt; SEQ ID NO: 2

93 &lt;211&gt; LENGTH: 508

E--&gt; 94 &lt;212&gt; TYPE: RPT

95 &lt;213&gt; ORGANISM: Homo sapiens

97 &lt;400&gt; SEQUENCE: 2

98 Met Thr Gln Thr Leu Lys Tyr Ala Ser Arg Val Phe His Arg Val Arg

99 1 5 10 15

100 Trp Ala Pro Glu Leu Gly Ala Ser Leu Gly Tyr Arg Glu Tyr His Ser

101 20 25 30

102 Ala Arg Arg Ser Leu Ala Asp Ile Pro Gly Pro Ser Thr Pro Ser Phe

103 35 40 45

104 Leu Ala Glu Leu Phe Cys Lys Gly Gly Leu Ser Arg Leu His Glu Leu

*Valid responses:*

- DNA

- RNA

- PRT

## RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/489,198

DATE: 06/14/2001

TIME: 10:13:12

Input Set : A:\Sequence.txt

Output Set: N:\CRF3\06142001\I489198.raw

105	50		55		60														
106	Gln	Val	Gln	Gly	Ala	Ala	His	Phe	Gly	Pro	Val	Trp	Leu	Ala	Ser	Phe			
107	65					70					75					80			
108	Gly	Thr	Val	Arg	Thr	Val	Tyr	Val	Ala	Ala	Pro	Ala	Leu	Val	Glu	Glu			
109					85					90					95				
110	Leu	Leu	Arg	Gln	Glu	Gly	Pro	Arg	Pro	Glu	Arg	Cys	Ser	Phe	Ser	Pro			
111				100					105				110						
112	Trp	Thr	Glu	His	Arg	Arg	Cys	Arg	Gln	Arg	Ala	Cys	Gly	Leu	Leu	Thr			
113			115					120					125						
114	Ala	Glu	Gly	Glu	Glu	Trp	Gln	Arg	Leu	Arg	Ser	Leu	Leu	Ala	Pro	Leu			
115		130					135					140							
116	Leu	Leu	Arg	Pro	Gln	Ala	Ala	Arg	Tyr	Ala	Gly	Thr	Leu	Asn	Asn				
117	145				150					155					160				
118	Val	Val	Cys	Asp	Leu	Val	Arg	Arg	Leu	Arg	Gln	Arg	Gly	Arg	Gly				
119				165					170				175						
120	Thr	Gly	Pro	Pro	Ala	Leu	Val	Arg	Asp	Val	Ala	Gly	Glu	Phe	Tyr	Lys			
121			180					185					190						
122	Phe	Gly	Leu	Glu	Gly	Ile	Ala	Ala	Val	Leu	Leu	Gly	Ser	Arg	Leu	Gly			
123			195				200					205							
124	Cys	Leu	Glu	Ala	Gln	Val	Pro	Pro	Asp	Thr	Glu	Thr	Phe	Ile	Arg	Ala			
125		210					215					220							
126	Val	Gly	Ser	Val	Phe	Val	Ser	Thr	Leu	Leu	Thr	Met	Ala	Met	Pro	His			
127	225				230					235					240				
128	Trp	Leu	Arg	His	Leu	Val	Pro	Gly	Pro	Trp	Gly	Arg	Leu	Cys	Arg	Asp			
129				245					250				255						
130	Trp	Asp	Gln	Met	Phe	Ala	Phe	Ala	Gln	Arg	His	Val	Glu	Arg	Arg	Glu			
131			260					265					270						
132	Ala	Glu	Ala	Ala	Met	Arg	Asn	Gly	Gly	Gln	Pro	Glu	Lys	Asp	Leu	Glu			
133			275				280					285							
134	Ser	Gly	Ala	His	Leu	Thr	His	Phe	Leu	Phe	Arg	Glu	Glu	Leu	Pro	Ala			
135		290					295					300							
136	Gln	Ser	Ile	Leu	Gly	Asn	Val	Thr	Glu	Leu	Leu	Ala	Gly	Val	Asp				
137	305				310					315				320					
138	Thr	Val	Ser	Asn	Thr	Leu	Ser	Trp	Ala	Leu	Tyr	Glu	Leu	Ser	Arg	His			
139				325					330				335						
140	Pro	Glu	Val	Gln	Thr	Ala	Leu	His	Ser	Glu	Ile	Thr	Ala	Ala	Leu	Ser			
141				340				345					350						
142	Pro	Gly	Ser	Ser	Ala	Tyr	Pro	Ser	Ala	Thr	Val	Leu	Ser	Gln	Leu	Pro			
143			355					360				365							
144	Leu	Leu	Lys	Ala	Val	Val	Lys	Glu	Val	Leu	Arg	Leu	Tyr	Pro	Val	Val			
145		370					375					380							
146	Pro	Gly	Asn	Ser	Arg	Val	Pro	Asp	Lys	Asp	Ile	His	Val	Gly	Asp	Tyr			
147	385				390					395				400					
148	Ile	Ile	Pro	Lys	Asn	Thr	Leu	Val	Thr	Leu	Cys	His	Tyr	Ala	Thr	Ser			
149				405					410				415						
150	Arg	Asp	Pro	Ala	Gln	Phe	Pro	Glu	Pro	Asn	Ser	Phe	Arg	Pro	Ala	Arg			
151				420					425				430						
152	Trp	Leu	Gly	Glu	Gly	Pro	Thr	Pro	His	Pro	Phe	Ala	Ser	Leu	Pro	Phe			
153			435					440					445						

## RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/489,198

DATE: 06/14/2001

TIME: 10:13:12

Input Set : A:\Sequence.txt

Output Set: N:\CRF3\06142001\I489198.raw

```
154 Gly Phe Gly Lys Arg Ser Cys Met Gly Arg Arg Leu Ala Glu Leu Glu
155      450                      455                      460
156 Leu Gln Met Ala Leu Ala Gln Ile Leu Thr His Phe Glu Val Gln Pro
157 465                      470                      475                      480
158 Glu Pro Gly Ala Ala Pro Val Arg Pro Lys Thr Arg Thr Val Leu Val
159      485                      490                      495
160 Pro Glu Arg Ser Ile Asn Leu Gln Phe Leu Asp Arg
161      500                      505
```



9/487, 198

p. 3

<210> 4  
<211> 2362  
<212> DNA  
<213> Homo sapiens

Seq. # 4

<220>  
<221> CDS  
<222> (1)...(1524)

There is an "n" at position 1926  
in sequence # 4. It is mandatory  
to have <220> to <223> features to  
explain what the "n" represents.  
See # 9 on the Error Summary  
Sheet.

## VERIFICATION SUMMARY

DATE: 06/14/2001

PATENT APPLICATION: US/09/489,198

TIME: 10:13:13

Input Set : A:\Sequence.txt

Output Set: N:\CRF3\06142001\I489198.raw

L:9 M:270 C: Current Application Number differs, Replaced Application Number  
L:10 M:271 C: Current Filing Date differs, Replaced Current Filing Date  
L:13 M:256 W: Invalid Numeric Header Field, Wrong Prior FILING DATE:YYYY-MM-DD  
L:21 M:310 E: (3) Wrong or Missing Sequence Type, TYPE:  
L:94 M:310 E: (3) Wrong or Missing Sequence Type, TYPE:  
L:399 M:258 W: Mandatory Feature missing, <223> not found for SEQ ID#:4  
L:399 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:4